WEST Search History

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DATE: Tuesday, April 06, 2004

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=ADJ		
☐	L5	L4 and phosphorothiolate	5
☐	L4	L3 and methylcytosine	717
☐	L3	L1 and (oligonucleotide or polynucleotide)	8659
☐	L2	L1 and oligonucleotide	8343
	DB=USPT; PLUR=YES; OP=ADJ		
☐	L1	(536/22.1,23.1,25.3,25.31,25.33)[CCLS]	9846

END OF SEARCH HISTORY

WEST Search History

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DATE: Tuesday, April 06, 2004

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L3	L2 and $nucleotide	76
☐	L2	L1 and phosphoramidite	76
☐	L1	phosphorothiolate	430

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 08:07:57 ON 06 APR 2004)

FILE 'AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUIRE, BABS, BIOCOMMERCE, BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CEN, CERAB, CIN, COMPENDEX, CONFSCI, COPPERLIT, CORROSION, DISSABS, ENCOMPLIT2, FEDRIP, GENBANK, INSPEC, INSPHYS, INVESTEXT, IPA, ...' ENTERED AT 08:09:57 ON 06 APR 2004

L1	1138923	S	OLIGONUCLEOTIDE
L2	302	S	L1 AND PHOSPHOROTHIOLATE
L3	5	S	L2 AND METHYLCYTOSINE

L3 ANSWER 1 OF 5 USPATFULL on STN
ACCESSION NUMBER: 2003:250623 USPATFULL
TITLE: Printing molecular library arrays
INVENTOR(S): Pease, R. Fabian, Stanford, CA, UNITED STATES
McGall, Glenn, San Jose, CA, UNITED STATES
Goldberg, Martin. J., Saratoga, CA, UNITED STATES
Rava, Richard P., Redwood City, CA, UNITED STATES
Fodor, Stephen P.A., Palo Alto, CA, UNITED STATES
Goss, Virginia, Santa Barbara, CA, UNITED STATES
Stryer, Lubert, Stanford, CA, UNITED STATES
Winkler, James L., San Diego, CA, UNITED STATES
PATENT ASSIGNEE(S): Affymetrix, Inc., Santa Clara, CA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003175409	A1	20030918
APPLICATION INFO.:	US 2003-387969	A1	20030313 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-841405, filed on 24 Apr 2001, PENDING Continuation of Ser. No. US 1999-427850, filed on 26 Oct 1999, GRANTED, Pat. No. US 6239273 Continuation of Ser. No. US 1998-93843, filed on 22 May 1998, ABANDONED Continuation of Ser. No. US 1996-635272, filed on 19 Apr 1996, GRANTED, Pat. No. US 5831070 Continuation of Ser. No. US 1995-395604, filed on 27 Feb 1995, GRANTED, Pat. No. US 5599695
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BANNER & WITCOFF, LTD., 28 STATE STREET, 28th FLOOR, BOSTON, MA, 02109-9601
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Page(s)
LINE COUNT: 1437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and apparatus for selectively applying a print material onto a substrate for the synthesis of an array of **oligonucleotides** at selected regions of a substrate. The print material includes a barrier material, a monomer sequence, a nucleoside, a deprotection. . .

SUMM . . . particular, one embodiment of the invention provides a method and associated apparatus for the selective application of an array of **oligonucleotides** on a substrate by way of standard dimethoxytrityl (DMT) based chemistry. The invention may be applied in the field of. . .

SUMM [0002] Industry utilizes or has proposed various techniques to synthesize arrays of **oligonucleotides**. One such technique is the use of small rubber tubes as reaction chambers to make up a single dimensional array. . . of polymer sequences for effective economical screening. A further limitation is an inability to form an array of, for example, **oligonucleotides** at selected regions of a substrate.

SUMM [0004] It would be desirable to have a method and apparatus for making high density arrays of **oligonucleotides** using DMT-based chemistry and other suitable **oligonucleotide** synthesis chemistries, as is a method and apparatus for conventional phosphoramidite-based synthesis of a spatially defined array of oligomers (e.g.,. . .

SUMM [0005] According to the present invention, a method and apparatus to form an array of polymers, such as **oligonucleotides** and related polymers (e.g., peptide nucleic acids) at selected regions of a substrate using conventional linkage chemistries (e.g., standard DMT-based **oligonucleotide** synthesis chemistry) is provided. The method and apparatus includes use of selected printing techniques in distributing materials such as barrier. . . Each of the printing techniques may be used in some embodiments with, for example, standard

DMT-based chemistry for synthesis of **oligonucleotides**, and in particular selected deprotecting agents in vapor form.

SUMM . . . method of forming polymers having diverse monomer sequences on a substrate. In an embodiment, the method is used to synthesize **oligonucleotides** having predetermined polynucleotide sequence(s) on a solid substrate, typically in the form of a spatially defined array, wherein the sequence(s) of an **oligonucleotide** is positionally determined. The present method includes steps of providing a substrate with a linker molecule layer thereon. The linker. . .

SUMM . . . provides a method for synthesizing a spatial array of polymers of diverse monomeric sequence (e.g., such as a collection of **oligonucleotides** having unique sequences), wherein the composition (e.g., nucleotide sequence) of each polymer is positionally defined by its location in the. . . defined portion of a substrate, said substrate optionally also comprising a layer of linker molecules and/or nascent polymers (e.g., nascent **oligonucleotides**), whereby the barrier material overlaying said first spatially defined portion of said substrate shields the underlying portion from contact with. . .

SUMM . . . jet print head or similar device. In an embodiment, the barrier material or reagent is suitable for use in polynucleotide (**oligonucleotide**) synthesis. In an embodiment, the substrate is a silicon or glass substrate or a charged membrane (e.g., nylon 66 or. . .

DRWD [0032] FIG. 26 illustrates a 2+2 array of **oligonucleotides** formed by masking out deprotection agents after A (vertical mask) and a first T in the synthesis of 3'-CGCATTCCG;

DRWD [0033] FIG. 27 is a scanned output of an array after hybridizing with 10 nM target **oligonucleotide** 5'-GCGTAGGC-fluorescein for 15 minutes at 15 C;

DETD . . . toxins and venoms, viral epitopes, hormones (e.g., opiates, steroids, etc.), hormone receptors, peptides, enzymes, enzyme substrates, cofactors, drugs, lectins, sugars, **oligonucleotides** , nucleic acids, oligosaccharides, proteins, and monoclonal antibodies.

DETD . . . d) Nucleic Acids: Sequences of nucleic acids may be synthesized to establish DNA or RNA binding sequences. Polynucleotides, which include **oligonucleotides**, are composed of nucleotides, typically linked 5' to 3' by a phosphodiester bond or **phosphorothiolate** bond or the like. The term "corresponds to" is used herein to mean that a polynucleotide sequence is homologous (i.e.,. . . of bases, including but not limited to: adenine, thymine, cytosine, guanine, uridine, inosine, deazaguanosine, N.sup.2-dimethylguanosine, 7-methylguanosine, N.sup.6-Δ.sup.2 isopentenyl-2-methylthioadenosine, 2'-O-methyladenine, 2'-O-methylthymine, 2'-O-**methylcytosine**, 2'-O-methylguanine, pseudouridine, dihydrouridine, 4-thiouridine, and the like.

DETD . . . etc.). For example and not to limit the invention, the following steps typically comprise a monomer additon cycle in phosphoramidite-based **oligonucleotide** synthesis: (1) deprotection, comprising removal of the DMT group from a 5'-protected nucleoside (which may be part of a nascent. . .

DETD . . . of the sequence as compared to the population of target polynucleotides, and chemical nature of the polynucleotide (e.g., methylphosphonate backbone, **phosphorothiolate**, etc.), among others.

DETD . . . agents in the vapor phase. This sequence of steps may be used for the selected synthesis of an array of **oligonucleotides**.

DETD . . . selected printing techniques to apply deprotection agents, barrier materials, nucleosides, and the like for the synthesis of an array of **oligonucleotides**. Preferably, the type of printing technique should be able to transfer a sufficient volume of print material to selected regions. . . easy, accurate, and cost effective manner. Examples of various printing techniques for the synthesis of for example an array of **oligonucleotides** are described herein.

Further examples of these embodiments of the present invention may be applied to the synthesis of arrays. . .

DETD . . . combinations thereof. Alternatively, the linkers may be the same molecule type as that being synthesized (i.e., nascent polymers), such as **oligonucleotides** or oligopeptides.

DETD . . . FIGS. 1-3 may be repeated to achieve the desired sequence of monomers at selected regions to form an array of **oligonucleotides**, peptides, other polymers, and the like.

DETD . . . crisp (and fine lined) to create an effective mask for printing a barrier pattern to obtain a diverse array of **oligonucleotides** .

DETD [0157] To demonstrate the effectiveness of the aforementioned techniques on the synthesis of **oligonucleotides**, selected experiments were performed. 2+2 arrays of **oligonucleotides** were prepared on substrates 1002 using silicon fragments (pieces of silicon material), which were electrostatically attached as crude masks at base #4 (A) and #5 (T). FIG. 26 illustrates a 2+2 array 1000 of **oligonucleotides** formed by masking out the deprotect agents after A (vertical mask 1009) and the first T in the synthesis of. . .

DETD . . . alternative constructions, and equivalents may be used. For example, while the description above is in terms of the synthesis of **oligonucleotide** arrays, it would be. possible to implement the present invention with peptides, small molecules, other polymers, or the like. Alternatively,. . .

CLM What is claimed is:

23. A method of synthesizing an **oligonucleotide** comprising the steps of: coupling a first portion of said **oligonucleotide** to said substrate, said first portion of said **oligonucleotide** comprising a removable protecting group; removing said protecting group with a vapor phase deprotection agent to expose a functional group on said first portion of said **oligonucleotide**; and covalently bonding a second portion of said **oligonucleotide** to said first portion of said **oligonucleotide**.

. . . method as recited in claim 24 further comprising repeating said removing and covalently bonding steps to form an array of **oligonucleotides**.

L3 ANSWER 2 OF 5 USPATFULL on STN

ACCESSION NUMBER:	2002:266436 USPATFULL
TITLE:	Printing **oligonucleotide** arrays
INVENTOR(S):	Pease, R. Fabian, Stanford, CA, UNITED STATES McGall, Glenn, Moutain View, CA, UNITED STATES Goldberg, Martin J., San Jose, CA, UNITED STATES Rava, Richard P., Palo Alto, CA, UNITED STATES Fodor, Stephen P.A., Palo Alto, CA, UNITED STATES Goss, Virginia, Santa Barbara, CA, UNITED STATES Stryer, Lubert, Stanford, CA, UNITED STATES Winkler, James L., Sunnyvale, CA, UNITED STATES
PATENT ASSIGNEE(S):	Affymetrix, Inc., Santa Clara, CA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002147319	A1	20021010
	US 6667394	B2	20031223
APPLICATION INFO.:	US 2001-841405	A1	20010424 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-427850, filed on 26 Oct 1999, GRANTED, Pat. No. US 6239273 Continuation of Ser. No. US 1998-93843, filed on 22 May 1998, ABANDONED Continuation of Ser. No. US 1996-634053, filed on 17 Apr 1996, GRANTED, Pat. No. US 5959098 Continuation of Ser. No. US 1995-395604, filed on 27 Feb 1995, GRANTED, Pat. No. US 5599695

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BANNER & WITCOFF, LTD., 28 STATE STREET, 28th FLOOR, BOSTON, MA, 02109
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Page(s)
LINE COUNT: 1437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Printing **oligonucleotide** arrays

AB A method and apparatus for selectively applying a print material onto a substrate for the synthesis of an array of **oligonucleotides** at selected regions of a substrate. The print material includes a barrier material, a monomer sequence, a nucleoside, a deprotection. . .

SUMM . . . particular, one embodiment of the invention provides a method and associated apparatus for the selective application of an array of **oligonucleotides** on a substrate by way of standard dimethoxytrityl (DMT) based chemistry. The invention may be applied in the field of. . .

SUMM [0002] Industry utilizes or has proposed various techniques to synthesize arrays of **oligonucleotides**. One such technique is the use of small rubber tubes as reaction chambers to make up a single dimensional array. . . of polymer sequences for effective economical screening. A further limitation is an inability to form an array of, for example, **oligonucleotides** at selected regions of a substrate.

SUMM [0004] It would be desirable to have a method and apparatus for making high density arrays of **oligonucleotides** using DMT-based chemistry and other suitable **oligonucleotide** synthesis chemistries, as is a method and apparatus for conventional phosphoramidite-based synthesis of a spatially defined array of oligomers (e.g.,. . .

SUMM [0005] According to the present invention, a method and apparatus to form an array of polymers, such as **oligonucleotides** and a substrate using conventional linkage chemistries (e.g., standard DMT-based **oligonucleotide** synthesis chemistry) is provided. The method and apparatus includes use of selected printing techniques in distributing materials such as barrier. . . Each of the printing techniques may be used in some embodiments with, for example, standard DMT-based chemistry for synthesis of **oligonucleotides**, and in particular selected deprotecting agents in vapor form.

SUMM . . . method of forming polymers having diverse monomer sequences on a substrate. In an embodiment, the method is used to synthesize **oligonucleotides** having predetermined polynucleotide sequence(s) on a solid substrate, typically in the form of a spatially defined array, wherein the sequence(s) of an **oligonucleotide** is positionally determined. The present method includes steps of providing a substrate with a linker molecule layer thereon. The linker. . .

SUMM . . . provides a method for synthesizing a spatial array of polymers of diverse monomeric sequence (e.g., such as a collection of **oligonucleotides** having unique sequences), wherein the composition (e.g., nucleotide sequence) of each polymer is positionally defined by its location in the. . . defined portion of a substrate, said substrate optionally also comprising a layer of linker molecules and/or nascent polymers (e.g., nascent **oligonucleotides**), whereby the barrier material overlaying said first spatially defined portion of said substrate shields the underlying portion from contact with. . .

SUMM . . . jet print head or similar device. In an embodiment, the barrier material or reagent is suitable for use in polynucleotide (**oligonucleotide**) synthesis. In an embodiment, the substrate is a silicon or glass substrate or a charged membrane (e.g., nylon 66 or. . .

DRWD [0032] FIG. 26 illustrates a 2+2 array of **oligonucleotides** formed by masking out deprotection agents after A (vertical mask) and a

first T in the synthesis of 3'-CGCATTCCG;

DRWD [0033] FIG. 27 is a scanned output of an array after hybridizing with 10 nM target **oligonucleotide** 5'-GCGTAGGC-fluorescein for 15 minutes at 15 C.;

DETD . . . toxins and venoms, viral epitopes, hormones (e.g., opiates, steroids, etc.), hormone receptors, peptides, enzymes, enzyme substrates, cofactors, drugs, lectins, sugars, **oligonucleotides**, nucleic acids, oligosaccharides, proteins, and monoclonal antibodies.

DETD [0045] d) Nucleic Acids: Sequences of nucleic acids may be Polynucleotides, which include **oligonucleotides**, are composed of nucleotides, typically linked 5' to 3' by a phosphodiester bond or **phosphorothiolate** bond or the like.

DETD . . . of bases, including but not limited to: adenine, thymine, cytosine, guanine, uridine, inosine, deazaguanosine, N.sup.2-dimethylguanosine, 7-methylguanosine, N.sup.6-Δ.sup.2 isopentenyl-2-methylthioadenosine, 2'-O-methyladenine, 2'-O-methylthymine, 2'-O-**methylcytosine**, 2'-O-methylguanine, pseudouridine, dihydrouridine, 4-thiouridine, and the like.

DETD . . . etc.). For example and not to limit the invention, the following steps typically comprise a monomer additon cycle in phosphoramidite-based **oligonucleotide** synthesis: (1) deprotection, comprising removal of the DMT group from a 5'-protected nucleoside (which may be part of a nascent. . .

DETD . . . of the sequence as compared to the population of target polynucleotides, and chemical nature of the polynucleotide (e.g., methylphosphonate backbone, **phosphorothiolate**, etc.), among others.

DETD . . . agents in the vapor phase. This sequence of steps may be used for the selected synthesis of an array of **oligonucleotides**.

DETD . . . selected printing techniques to apply deprotection agents, barrier materials, nucleosides, and the like for the synthesis of an array of **oligonucleotides**. Preferably, the type of printing technique should be able to transfer a sufficient volume of print material to selected regions. . . easy, accurate, and cost effective manner. Examples of various printing techniques for the synthesis of for example an array of **oligonucleotides** are described herein. Further examples of these embodiments of the present invention may be applied to the synthesis of arrays. . .

DETD . . . combinations thereof. Alternatively, the linkers may be the same molecule type as that being synthesized (i.e., nascent polymers), such as **oligonucleotides** or oligopeptides.

DETD . . . FIGS. 1-3 may be repeated to achieve the desired sequence of monomers at selected regions to form an array of **oligonucleotides**, peptides, other polymers, and the like.

DETD . . . crisp (and fine lined) to create an effective mask for printing a barrier pattern to obtain a diverse array of **oligonucleotides**.

DETD [0156] To demonstrate the effectiveness of the aforementioned techniques on the synthesis of **oligonucleotides**, selected experiments were performed. 2+2 arrays of **oligonucleotides** were prepared on substrates 1002 using silicon fragments (pieces of silicon material), which were electrostatically attached as crude masks at base #4 (A) and #5 (T). FIG. 26 illustrates a 2+2 array 1000 of **oligonucleotides** formed by masking out the deprotect agents after A (vertical mask 1009) and the first T in the synthesis of. . .

DETD . . . alternative constructions, and equivalents may be used. For example, while the description above is in terms of the synthesis of **oligonucleotide** arrays, it would be possible to implement the present invention with peptides, small molecules, other polymers, or the like. Alternatively,. . .

CLM What is claimed is:

23. A method of synthesizing an **oligonucleotide** comprising the steps of: coupling a first portion of said **oligonucleotide** to said substrate, said first portion of said **oligonucleotide**

comprising a removable protecting group; removing said protecting group with a vapor phase deprotection agent to expose a functional group on said first portion of said **oligonucleotide**; and covalently bonding a second portion of said **oligonucleotide** to said first portion of said **oligonucleotide**.

. . . method as recited in claim 24 further comprising repeating said removing and covalently bonding steps to form an array of **oligonucleotides**.

L3 ANSWER 3 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2001:79297 USPATFULL

TITLE: Printing molecular library arrays

INVENTOR(S): Pease, R. Fabian, Stanford, CA, United States
McGall, Glenn, Mountain View, CA, United States
Goldberg, Martin J., San Jose, CA, United States
Rava, Richard P., Palo Alto, CA, United States
Fodor, Stephen P. A., Palo Alto, CA, United States
Goss, Virginia, Santa Barbara, CA, United States
Stryer, Lubert, Stanford, CA, United States
Winkler, James L., Sunnyvale, CA, United States

PATENT ASSIGNEE(S): Affymetrix, Inc., Santa Clara, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6239273	B1	20010529
APPLICATION INFO.:	US 1999-427850		19991026 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-93843, filed on 22 May 1998, now abandoned Continuation of Ser. No. US 1996-634053, filed on 17 Apr 1996, now patented, Pat. No. US 5959098 Continuation of Ser. No. US 1995-395604, filed on 27 Feb 1995, now patented, Pat. No. US 5599695

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fredman, Jeffrey
LEGAL REPRESENTATIVE: Banner & Witcoff, Ltd.
NUMBER OF CLAIMS: 39
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 32 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 1616
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and apparatus for selectively applying a print material onto a substrate for the synthesis of an array of **oligonucleotides** at selected regions of a substrate. The print material includes a barrier material, a monomer sequence, a nucleoside, a deprotection. . .

SUMM . . . particular, one embodiment of the invention provides a method and associated apparatus for the selective application of an array of **oligonucleotides** on a substrate by way of standard dimethoxytrityl (DMT) based chemistry. The invention may be applied in the field of. . .

SUMM Industry utilizes or has proposed various techniques to synthesize arrays of **oligonucleotides**. One such technique is the use of small rubber tubes as reaction chambers to make up a single dimensional array. . . of polymer sequences for effective economical screening. A further limitation is an inability to form an array of, for example, **oligonucleotides** at selected regions of a substrate.

SUMM It would be desirable to have a method and apparatus for making high density arrays of **oligonucleotides** using DMT-based chemistry and other suitable **oligonucleotide** synthesis chemistries, as is a method and apparatus for conventional phosphoramidite-based synthesis of a spatially defined array of oligomers (e.g.,. . .

SUMM . . . and related polymers (e.g., peptide nucleic acids) at selected

regions of a substrate using conventional linkage chemistries (e.g., standard DMT-based **oligonucleotide** synthesis chemistry) is provided. The method and apparatus includes use of selected printing techniques in distributing materials such as barrier. . . Each of the printing techniques may be used in some embodiments with, for example, standard DMT-based chemistry for synthesis of **oligonucleotides** , and in particular selected deprotecting agents in vapor form.

SUMM . . . method of forming polymers having diverse monomer sequences on a substrate. In an embodiment, the method is used to synthesize **oligonucleotides** having predetermined polynucleotide sequence(s) on a solid substrate, typically in the form of a spatially defined array, wherein the sequence(s) of an **oligonucleotide** is positionally determined. The present method includes steps of providing a substrate with a linker molecule layer thereon. The linker. . .

SUMM . . . provides a method for synthesizing a spatial array of polymers of diverse monomeric sequence (e.g., such as a collection of **oligonucleotides** having unique sequences), wherein the composition (e.g., nucleotide sequence) of each polymer is positionally defined by its location in the. . . defined portion of a substrate, said substrate optionally also comprising a layer of linker molecules and/or nascent polymers (e.g., nascent **oligonucleotides**), whereby the barrier material overlaying said first spatially defined portion of said substrate shields the underlying portion from contact with. . .

SUMM . . . jet print head or similar device. In an embodiment, the barrier material or reagent is suitable for use in polynucleotide (**oligonucleotide**) synthesis. In an embodiment, the substrate is a silicon or glass substrate or a charged membrane (e.g., nylon 66 or. . .

DRWD FIG. 26 illustrates a 2+2 array of **oligonucleotides** formed by masking out deprotection agents after A (vertical mask) and a first T in the synthesis of 3'-CGCATTCCG;

DRWD FIG. 27 is a scanned output of an array after hybridizing with 10 nM target **oligonucleotide** 5'-GCGTAGGC-fluorescein for 15 minutes at 15 C.;

DETD . . . toxins and venoms, viral epitopes, hormones (e.g., opiates, steroids, etc.), hormone receptors, peptides, enzymes, enzyme substrates, cofactors, drugs, lectins, sugars, **oligonucleotides** , nucleic acids, oligosaccharides, proteins, and monoclonal antibodies.

DETD d) Nucleic Acids: Sequences of nucleicacids may be synthesized to establish DNA or RNA binding sequences. Polynucleotides, which include **oligonucleotides**, are composed of nucleotides, typically linked 5' to 3' by a phosphodiester bond or **phosphorothiolate** bond or the like.

DETD . . . including but not limited to: adenine, thymine, cytosine, guanine, uridine, inosine, deazaguanosine, N.sup.2 -dimethylguanosine, 7-methylguanosine, N.sup.6 -Δ.sup.2 isopentenyl-2-methylthioadenosine, 2'-O-methyladenine, 2'-O-methylthymine, 2'-O-**methylcytosine**, 2'-O-methylguanine, pseudouridine, dihydrouridine, 4-thiouridine, and the like.

DETD . . . etc.). For example and not to limit the invention, the following steps typically comprise a monomer addition cycle in phosphoramidite-based **oligonucleotide** synthesis: (1) deprotection, comprising removal of the DMT group from a 5'-protected nucleoside (which may be part of a nascent. . .

DETD . . .. of the sequence as compared to the population of target polynucleotides, and chemical nature of the polynucleotide (e.g., methylphosphonate backbone, **phosphorothiolate**, etc.), among others.

DETD . . . agents in the vapor phase. This sequence of steps may be used for the selected synthesis of an array of **oligonucleotides**.

DETD . . . selected printing techniques to apply deprotection agents, barrier materials, nucleosides, and the like for the synthesis of an array of **oligonucleotides**. Preferably, the type of printing

technique should be able to transfer a sufficient volume of print material to selected regions. . . . easy, accurate, and cost effective manner. Examples of various printing techniques for the synthesis of for example an array of **oligonucleotides** are described herein. Further examples of these embodiments of the present invention may be applied to the synthesis of arrays. . .

DETD . . . combinations thereof. Alternatively, the linkers may be the same molecule type as that being synthesized (i.e., nascent polymers), such as **oligonucleotides** or oligopeptides.

DETD . . . FIGS. 1-3 may be repeated to achieve the desired sequence of monomers at selected regions to form an array of **oligonucleotides**, peptides, other polymers, and the like.

DETD . . . crisp (and fine lined) to create an effective mask for printing a barrier pattern to obtain a diverse array of **oligonucleotides** .

DETD To demonstrate the effectiveness of the aforementioned techniques on the synthesis of **oligonucleotides**, selected experiments were performed. 2+2 arrays of **oligonucleotides** were prepared on substrates 1002 using silicon fragments (pieces of silicon material), which were electrostatically attached as crude masks at base #4 (A) and #5 (T). FIG. 26 illustrates a 2+2 array 1000 of **oligonucleotides** formed by masking out the deprotect agents after A (vertical mask 1009) and the first T in the synthesis of. . .

DETD . . . alternative constructions, and equivalents may be used. For example, while the description above is in terms of the synthesis of **oligonucleotide** arrays, it would be possible to implement the present invention with peptides, small molecules, other polymers, or the like. Alternatively,. . .

CLM What is claimed is:

15. The method of claim 1, wherein the polymer is selected from the group consisting of: nucleic acids, polynucleotides, **oligonucleotides**, polypeptides, polysaccharides, oligosaccharides, phospholipids, polyurethanes, polyesters, polycarbonates, polyureas, polyamides, polyethyleneimines, polyarylene sulfides, polysiloxanes, polyimides, and polyacetates.

16. The method of claim 1, wherein said polymer is selected from the group consisting of: nucleic acids, polynucleotides, **oligonucleotides**, polypeptides, and polysaccharides.

33. A method of synthesizing a nucleic acid or a polynucleotide comprising the steps of: a) providing an **oligonucleotide** having a proximal end and a distal end, said proximal end coupled to a substrate having a surface, and said. . . group with a deprotection agent solely in vapor phase solely to expose a functional group; and c) covalently bonding an **oligonucleotide** to said exposed fumctional group.

34. The method of claim 33, wherein the **oligonucleotide** of step c) has a proximal end and a distal end, the proximal end is bonded to said exposed functional. . .

35. The method of claim 33, wherein in step a), a plurality of **oligonucleotides** are coupled to the substrate to form an array.

L3 ANSWER 4 OF 5 USPATFULL on STN

ACCESSION NUMBER: 1998:135211 USPATFULL

TITLE: Printing **oligonucleotide** arrays using deprotection agents solely in the vapor phase

INVENTOR(S): Pease, R. Fabian, Stanford, CA, United States
McGall, Glenn, Mountain View, CA, United States
Goldberg, Martin J., San Jose, CA, United States
Rava, Richard P., Palo Alto, CA, United States
Fodor, Stephen P. A., Palo Alto, CA, United States

Goss, Virginia, Santa Barbara, CA, United States
Stryer, Lubert, Stanford, CA, United States
Winkler, James L., Sunyvale, CA, United States
PATENT ASSIGNEE(S): Affymetrix, Inc., Santa Clara, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5831070		19981103
APPLICATION INFO.:	US 1996-635272		19960419 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-395604, filed on 27 Feb 1995, now patented, Pat. No. US 5559695

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jones, W. Gary
ASSISTANT EXAMINER: Fredman, Jeffrey
LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 32 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 1410
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Printing **oligonucleotide** arrays using deprotection agents solely in the vapor phase

AB A method and apparatus for selectively applying a print material onto a substrate for the synthesis of an array of **oligonucleotides** at selected regions of a substrate. The print material includes a barrier material, a monomer sequence, a nucleoside, a deprotection. . .

SUMM . . . particular, one embodiment of the invention provides a method and associated apparatus for the selective application of an array of **oligonucleotides** on a substrate by way of standard dimethoxytrityl (DMT) based chemistry. The invention may be applied in the field of. . .

SUMM Industry utilizes or has proposed various techniques to synthesize arrays of **oligonucleotides**. One such technique is the use of small rubber tubes as reaction chambers to make up a single dimensional array. . .

SUMM It would be desirable to have a method and apparatus for making high density arrays of **oligonucleotides** using DMT-based chemistry and other suitable **oligonucleotide** synthesis chemistries, as is a method and apparatus for conventional phosphoramidite-based synthesis of a spatially defined array of oligomers (e.g.,. . .

SUMM According to the present invention , a method and apparatus to form an array of polymers, such as **oligonucleotides** and related polymers (e.g., peptide nucleic acids) at selected regions of a substrate using conventional linkage chemistries (e.g., standard DMT-based **oligonucleotide** synthesis chemistry) is provided. The method and apparatus includes use of selected printing techniques in distributing materials such as barrier. . . Each of the printing techniques may be used in some embodiments with, for example, standard DMT-based chemistry for synthesis of **oligonucleotides**, and in particular selected deprotecting agents in vapor form.

SUMM . . . method of forming polymers having diverse monomer sequences on a substrate. In an embodiment, the method is used to synthesize **oligonucleotides** having predetermined polynucleotide sequence(s) on a solid substrate, typically in the form of a spatially defined array, wherein the sequence(s) of an **oligonucleotide** is positionally determined. The present method includes steps of providing a substrate with a linker molecule layer thereon. The linker. . .

SUMM . . . provides a method for synthesizing a spatial array of polymers of diverse monomeric sequence (e.g., such as a collection of **oligonucleotides** having unique sequences), wherein the composition (e.g., nucleotide sequence) of each polymer is positionally defined by its location in the. . . defined portion of a substrate,

said substrate optionally also comprising a layer of linker molecules and/or nascent polymers (e.g., nascent **oligonucleotides**), whereby the barrier material overlaying said first spatially defined portion of said substrate shields the underlying portion from contact with. . .

SUMM . . . jet print head or similar device. In an embodiment, the barrier material or reagent is suitable for use in polynucleotide (**oligonucleotide**) synthesis. In an embodiment, the substrate is a silicon or glass substrate or a charged membrane (e.g., nylon 66 or. . .

DRWD FIG. 26 illustrates a 2+2 array of **oligonucleotides** formed by masking out deprotection agents after A (vertical mask) and a first T in the synthesis of 3'-CGCATTCCG;

DRWD FIG. 27 is a scanned output of an array after hybridizing with 10 nM target **oligonucleotide** 5'-GCGTAGGC-fluorescein for 15 minutes at 15° C.;

DETD . . . toxins and venoms, viral epitopes, hormones (e.g., opiates, steroids, etc.), hormone receptors, peptides, enzymes, enzyme substrates, cofactors, drugs, lectins, sugars, **oligonucleotides** , nucleic acids, oligosaccharides, proteins, and monoclonal antibodies.

DETD d) Nucleic Acids: Sequences of nucleic acids may be synthesize to establish DNA or RNA binding sequences. Polynucleotides, which include **oligonucleotides**, are composed of nucleotides, typically linked 5' to 3' by a phosphodiester bond or **phosphorothiolate** bond or the like.

DETD . . . including but not limited to: adenine, thymine, cytosine, guanine, uridine, inosine, deazaguanosine, N.sup.2 -dimethylguanosine, 7-methylguanosine, N.sup.6 -Δ.sup.2 isopentenyl-2-methylthioadenosine, 2'-O-methyladenine, 2'-O-methylthymine, 2'-O-**methylcytosine**, 2'-O-methylguanine, pseudouridine, dihydrouridine, 4-thiouridine, and the like.

DETD . . . etc.). For example and not to limit the invention, the following steps typically comprise a monomer addition cycle in phosphoramidite-based **oligonucleotide** synthesis: (1) deprotection, comprising removal of the DMT group from a 5'-protected nucleoside (which may be part of a nascent. . .

DETD . . . of the sequence as compared to the population of target polynucleotides, and chemical nature of the polynucleotide (e.g., methylphosphonate backbone, **phosphorothiolate**, etc.), among others.

DETD . . . agents in the vapor phase. This sequence of steps may be used for the selected synthesis of an array of **oligonucleotides**.

DETD . . . selected printing techniques to apply deprotection agents, barrier materials, nucleosides, and the like for the synthesis of an array of **oligonucleotides**. Preferably, the type of printing technique should be able to transfer a sufficient volume of print material to selected regions. . . easy, accurate, and cost effective manner. Examples of various printing techniques for the synthesis of for example an array of **oligonucleotides** are described herein. Further examples of these embodiments of the present invention may be applied to the synthesis of arrays. . .

DETD . . . combinations thereof. Alternatively, the linkers may be the same molecule type as that being synthesized (i.e., nascent polymers), such as **oligonucleotides** or oligopeptides.

DETD . . . FIGS. 1-3 may be repeated to achieve the desired sequence of monomers at selected regions to form an array of **oligonucleotides**, peptides, other polymers, and the like.

DETD . . . crisp (and fine lined) to create an effective mask for printing a barrier pattern to obtain a diverse array of **oligonucleotides** .

DETD To demonstrate the effectiveness of the aforementioned techniques on the synthesis of **oligonucleotides**, selected experiments were performed. 2+2 arrays of **oligonucleotides** were prepared on substrates 1002 using silicon fragments (pieces of silicon material),

which were electrostatically attached as crude masks at base #4 (A) and #5 (T). FIG. 26 illustrates a 2+2 array 1000 of **oligonucleotides** formed by masking out the deprotect agents after A (vertical mask 1009) and the first T in the synthesis of. . .

DETD . . . alternative constructions, and equivalents may be used. For example, while the description above is in terms of the synthesis of **oligonucleotide** arrays, it would be possible to implement the present invention with peptides, small molecules, other polymers, or the like. Alternatively,. . .

CLM What is claimed is:

5. A method of synthesizing an **oligonucleotide** comprising the steps of: coupling a first portion of said **oligonucleotide** to said substrate, said first portion of said **oligonucleotide** comprising a removable protecting group; removing said protecting group with a deprotection agent in a vapor phase to expose a functional group on said first portion of said **oligonucleotide**, wherein said surface of said substrate is selectively protected by a mask; and covalently bonding a second portion of said **oligonucleotide** to said first portion of said **oligonucleotide**.

L3 ANSWER 5 OF 5 USPATFULL on STN

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SUMM Industry utilizes or has proposed various techniques to synthesize arrays of **oligonucleotides**. One such technique is the use of small rubber tubes as reaction chambers to make up a single dimensional array. . . of polymer sequences for effective economical screening. A further limitation is an inability to form an array of, for example,

oligonucleotides at selected regions of a substrate.

SUMM It would be desirable to have a method and apparatus for making high density arrays of **oligonucleotides** using DMT-based chemistry and other suitable **oligonucleotide** synthesis chemistries, as is a method and apparatus for conventional phosphoramidite-based synthesis of a spatially defined array of oligomers (e.g.,. . .

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CLM What is claimed is:

19. A method of synthesizing an **oligonucleotide** comprising the steps of: coupling a first portion of said **oligonucleotide** to said substrate, said first portion of said **oligonucleotide** comprising a removable protecting group; solely removing said protecting group with a deprotection agent solely in a vapor phase to expose a functional group on said first portion of said **oligonucleotide** ; and covalently bonding a second portion of said **oligonucleotide** to said first portion of said **oligonucleotide**.

. . . method as recited in claim 20 further comprising repeating said removing and covalently bonding steps to form an array of **oligonucleotides**.

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